Declarations of Interest

All experts and resource advisers invited to participate in the meeting completed beforehand the WHO standard form for declaration of interests. At the start of the meeting, all participants were asked to confirm their interests, and to provide any additional information relevant to the subject matter of the meeting. No conflicts of interest were identified.

Definitions

Foodborne disease

A foodborne disease (FBD) can be defined as a disease commonly transmitted through ingested food. FBDs comprise a broad group of illnesses, and may be caused by microbial pathogens, parasites, chemical contaminants and biotoxins.

Burden of disease

In the context of this Initiative, the term "burden of disease" follows the principles of the Global Burden of Disease Study, and includes the quantification of morbidity, all disabling complications and mortality in a single summary measure (DALY).

DALY (disability-adjusted life year)

A health gap measure that combines the years of life lost due to premature death and the years lived with disability from a disease or condition, for varying degrees of severity, making time itself the common metric for death and disability. One DALY equates to one year of healthy life lost.

The table below shows the main elements that are needed to arrive at burden estimates expressed in DALYs.

Food

According to the Codex Alimentarius Commission, "food means any substance, whether processed, semi-processed or raw, which is intended for human consumption, and includes drink, chewing gum and any substance which has been used in the manufacture, preparation or treatment of food but does not include cosmetics or tobacco or substances used only as drugs"(1). The definition includes all bottled drinks.

1. Introduction

This report summarizes the discussions during the fifth meeting of the Foodborne Disease Burden Epidemiology Reference Group (FERG) on 8–12 April 2013, and related meetings, at the World Health Organization (WHO) Headquarters in Geneva, Switzerland. This was the final meeting of the entire FERG and it is envisioned that the foodborne burden of disease estimates will be released in 2015. The participants are listed in Annex 1.

Dr Kazuaki Miyagishima, Director, WHO Department of Food Safety and Zoonoses, opened the meeting. Professor Arie Havelaar reviewed the history of FERG since its inception in 2006, and outlined the aims of the current meeting (FERG5). Dr Rob Lake presented the agenda.

1.1 Objectives of the meeting

The objectives of the meeting were:

- to present the final results of the systematic reviews commissioned by the task forces on enteric diseases, parasitic diseases and chemicals and toxins;
- to develop preliminary estimates of the global and regional burden of foodborne disease (FBD), through joint discussions between the hazard task forces and the Computational Task Force (CTF); and
- to review the status of country studies and identify additional tools and training resources for situation analysis and knowledge translation.

2. Objectives and organizational structure of FERG

2.1 Objectives of FERG

FERG acts as an advisory body to WHO on global epidemiology of foodborne diseases. FERG was established in 2006, at which time foodborne disease was not included as a risk factor in the Global Burden of Diseases Study.

The objectives of FERG are to:

- assemble, appraise and report on estimates of the current, projected and averted burden of foodborne disease;
- conduct epidemiological reviews of the mortality, morbidity and disability associated with each of the major foodborne diseases;
- devise models for the estimation of FBD burden where data are lacking;
- develop source attribution models to estimate what proportion of each disease is foodborne; and, most importantly
- use the devised models to develop user-friendly tools for studies of burden of foodborne disease at country level.
- Furthermore, the initiative aims to:
- strengthen the capacity of countries to assess burden of foodborne disease and encourage countries to undertake a study of burden of foodborne disease;
- encourage countries to use burden of foodborne disease estimates to set evidence-informed policies;
- provide estimates of the global burden of foodborne diseases, according to age, sex and region, for a defined list of causative agents of microbial, parasitic, and chemical origin.

In estimating the global human health burden, expressed in disability-adjusted life years (DALYs), FERG has considered microbial, parasitic, and chemical contamination of food, and has specifically focused on diseases whose incidence and severity are thought to be high and on pathogens and chemicals that are most likely to contaminate food and that are preventable. Initially, FERG was intended to be a 5-year project, from 2007 to 2012. The current aim of FERG is to publish the estimates of the global burden of foodborne disease in 2014.

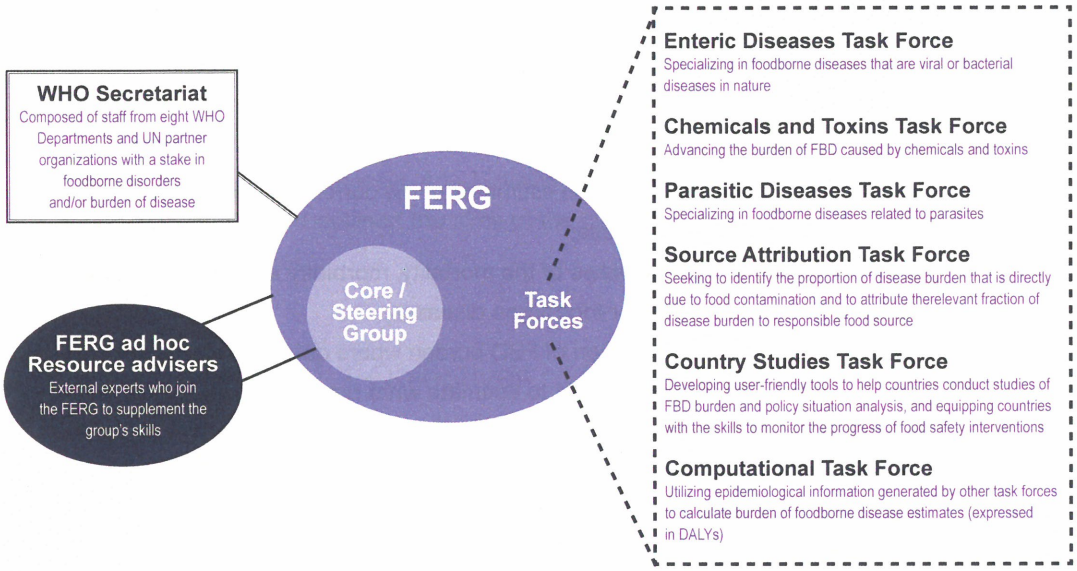
2.2 Organizational structure of FERG

FERG consists of: a Core (or Steering) Group, which coordinates and oversees the scientific work; six thematic task forces, which work in specific areas, as shown in Figure 1; and external resource and technical advisers, who are invited on an ad hoc basis to provide specific expertise.

In March 2012, the sixth task force – the Computational Task Force – was established, with the overall aim of advising and assisting WHO in converting into DALYs the results

of (a) the global epidemiological reviews of mortality, morbidity and disability associated with each of the major foodborne diseases, and (b) the epidemiological data resulting from the FERG country studies.

Figure 1. Organizational structure of FERG



3. Global Burden of Disease Study 2010

In December 2012, the results of the Global Burden of Diseases, Injuries, and Risk Factors Study 2010 (GBD 2010) were published (2) This study estimated the burden of premature death and disability due to 291 diseases and injuries, 1160 sequelae, and 67 risk factors, for 20 age groups and both sexes, in 1990, 2005 and 2010. Estimates were produced for 187 countries and 21 regions.

The GBD 2010 estimates are not official WHO estimates, but this does not mean that they cannot be used by WHO programmes. However, the Organization has concerns about the results, particularly for the WHO priority diseases, such as human immunodeficiency virus (HIV) infection and malaria. WHO will continue to produce its own estimates for these diseases, which will be less detailed than the GBD estimates. WHO intends to produce regular updates of causes of death, with the next one expected by the end of 2013. Furthermore, WHO will continue to estimate DALYs. There is a clear consensus that the burden of disease concept and the DALY metric are useful and important for some programmes. For estimates of years lived with a disability (YLD), WHO will draw on GBD estimates, except when there is reason to believe that the estimates are not valid or improved models are available. WHO will not revise all the GBD 2010 estimates, but will revise estimates for certain diseases, particularly environmental diseases.

The estimates of WHO and GBD 2010 for total diarrhoeal disease are comparable, but there are differences in distribution by etiology. A group should be formed to discuss the reasons for the differences and consistency checks should be made if possible. The official WHO estimates should be updated by the end of 2013.

WHO has advised that DisMod-MR, the software that was used for burden of disease analysis for regional, national and subnational populations in GBD 2010, should not be used for FERG estimates, because it is undocumented and not in the public domain.

New disability weights were derived for GBD 2010. WHO considers that these disability weights are generally consistent, although those for sensory impairments are very low in comparison with previously derived disability weights. WHO recommends using the GBD 2010 disability weights, unless there is a good reason not to, e.g. if there is a discrepancy between the health states included in the epidemiological data and the health states reflected by the disability weight. There will be a follow-up of the disability weight Internet survey in 2013 to validate the GBD 2010 disability weights.

4. Enteric Disease Task Force

Initially, the Enteric Disease Task Force (EDTF) planned to estimate the burden of disease associated with 30 enteric agents. However, during the FERG meeting in Albania in 2011, it was decided to focus on 18 priority agents.

The EDTF held a meeting immediately prior to FERG5, in order to:

- discuss the status of the systematic reviews of enteric diseases;
- review, modify, simplify and reach agreement on the disease models of the agents;
- liaise with the Computational Task Force to discuss how to proceed for each of the agents;
- consult the Source Attribution Task Force to discuss the expert panels.

4.1 Diarrhoeal diseases and sequelae

The project on Interactions of Malnutrition & Enteric Infections: Consequences for Child Health and Development (MAL-ED) and the Global Enteric Multicenter Study may have additional information on the fraction of diarrhoeal cases that can be attributed to certain agents, and on the existence of other sequelae; this should be followed up (3, 4).

The EDTF decided that, with a few exceptions, diarrhoeal diseases have moderate illness as an outcome (i.e. infections would not be divided into mild, moderate and severe). The exceptions are Salmonella infection (which includes invasive infections), Shiga-toxin-producing Escherichia coli (STEC) (which includes haemolytic uraemic syndrome (HUS) and end-stage renal disease (ESRD)), and Campylobacter infection (which includes Guillain-Barré syndrome). Furthermore, the EDTF simplified the models of diarrhoeal diseases, to exclude reactive arthritis, inflammatory bowel disease and irritable bowel syndrome, because data on these outcomes are scarce, particularly in low-resource countries.

4.1.1 *Campylobacter*

The disease model of *Campylobacter* has been simplified. The health outcomes now included are diarrhoea and Guillain-Barré syndrome. In order to estimate the incidence of Guillain-Barré syndrome, an estimate of all Guillain-Barré cases will first be constructed and subsequently the number of cases due to *Campylobacter* will be estimated. A systematic review has been performed on the association between *Campylobacter* and Guillain-Barré syndrome (5). Several items of work related to this issue, including the global estimate of Guillain-Barré syndrome and the fatality rate for Guillain-Barré syndrome, will be followed up.

To estimate the burden of disease, data on duration, severity and case-fatality in low- and high-income settings are needed, as well as on residual symptoms.

4.1.2 Typhoid and paratyphoid fever

A review and critique of alternative estimates of typhoid and paratyphoid fever were presented during the meeting of the EDTF. The methods and results of three studies of typhoid or paratyphoid fever were summarized and critically reviewed : (1) Johns Hopkins University 2010 (6); (2) International Vaccine Institute 2010 (7) and (3) the Institute for Health Metrics and Evaluation (IHME) Global Burden of Disease Study 2010 (2). All the approaches had strong points and shortcomings, but on balance the GBD 2010 approach was recommended, despite the opacity of its methods. The task force agreed to adopt the GBD 2010 typhoid estimates, but will consult the WHO typhoid group to determine if they have any potential concerns. IHME will need to be contacted to provide estimates of incidence.

4.1.3 Non-invasive and invasive Salmonella infection

Invasive *Salmonella* infection has very different symptoms from non-invasive infection. After some discussion, the Task Force decided that severe acute infectious disease is a good proxy for invasive Salmonella. The EDTF decided to combine the *Salmonella* estimates from the commissioned study by Pires, which includes the estimates of the Child Health Epidemiology Reference Group (CHERG), with those generated from a systematic review on invasive salmonellosis by Crump and Ao (unpublished work). Crump has agreed to provide recommendations on appropriate disability weights and case-fatality rate for invasive salmonellosis.

There are co-morbidity issues related to invasive salmonellosis, malaria and HIV infection. It is not clear how deaths associated with this situation should be counted. Should all deaths be counted as invasive salmonella deaths? Or should there be a correction for co-morbidities by, for instance, comparing the figures with those for AIDS deaths in areas where invasive salmonellosis is less significant? This may also be an issue for other agents, and a consistent approach is needed.

Separate source attribution for invasive and non-invasive salmonellosis is not needed.

4.1.4 *Mycobacterium bovis*

To arrive at estimates for the burden of *Mycobacterium* bovis infection, the EDTF will use WHO estimates of human tuberculosis, and assume that approximately 1% (or exact value to be taken from the systematic review) of tuberculosis cases are caused by *M. bovis* and that 100% of those are foodborne. The assumption of 1% *M. bovis* infections is likely to be conservative. However, because of difficulties associated with microscopy and culture of *M. bovis*, this is appropriate at this point. The next step is to obtain a list of *M. bovis*-free countries from the World Organisation for Animal Health.

4.1.5 Brucellosis

The systematic review of brucellosis by Dean et al. (8) gives the incidence of brucellosis in various countries. These data will be transferred to the CTF for imputation. The US Centers for Disease Control and Prevention (CDC) will be consulted to explore the possibility of using alternative approaches to extrapolation to generate additional estimates and check the validity of the results produced by the CTF imputation. If the CDC project

is not feasible, colleagues from both CDC and WHO are willing to review the estimates generated by the CTF. Currently there is no disease model for brucellosis, but the EDTF will provide such a model within two months.

4.1.6 *Listeria*

A systematic review and a multilevel meta-analysis were conducted to calculate incidence of listeriosis and distribution of outcomes by WHO subregion and by age group. So far, the incidence of listeriosis has been calculated for 7 of the 14 WHO subregions and work is continuing. If estimates cannot be obtained for all WHO subregions, only well established, published national estimates will be used (e.g. from the USA, Canada and various countries in Europe). Countries with no estimates will be left out of further calculations. This fallback position will ensure that listeriosis is not completely ignored, while at the same time avoiding unjustifiable extrapolations that might detract from the message.

In the coming months the EDTF will collect information from the countries that have well established estimates for listeriosis. It will also collect less well validated data from other countries and try to extrapolate them. Furthermore, resource advisers will consult with the WHO Meningitis Group to explore if the CHERG estimates of meningitis deaths and cases can be used to estimate those associated with Listeria. The health outcomes of *Listeria* infection are septicaemia and meningitis. Meningitis may also cause residual disability, such as hearing problems and cognitive impairments. A variable case-fatality rate for meningitis will be used for developed and developing countries, and a strategy will need to be devised to ascertain these case-fatality rates. Expert elicitation is not needed for attribution of listeriosis, because it is 100% foodborne; attribution to food type will be included in the expert attribution study.

4.1.7 STEC

The STEC disease model includes diarrhoeal disease, haemolytic uraemic syndrome and end-stage renal disease. Proxy disability weights are needed for haemolytic uraemic syndrome. Data are also needed on duration, severity and case-fatality in high- and low-income settings, for both haemolytic uraemic syndrome and end-stage renal disease. For the calculation of the burden of disease due to ESRD, countries will be divided according to whether the population has good or poor access to health care. Without health care, a patient with ESRD will die. With health care, there will be a long-term impact on health-related quality of life that is difficult to assess. There are ESRD models from the Netherlands and the USA.

The probability of developing haemolytic uraemic syndrome is different for different types of STEC, and the distribution of STEC types varies by region. A systematic review of STEC has been performed, and will provide data on incidence, and the numbers of cases of acute illness, HUS, ESRD, and deaths. It is not clear how the other data will be obtained.

4.1.8 Bacterial toxins

The EDTF decided not to remove toxins from the list of hazards being considered at this point, since doing so might mean that they would be neglected in the future. The EDTF

will attempt to collect and compile all readily available incidence data on intoxications from countries and subsequently explore if the CTF imputation tool can be used. CDC will conduct a quick systematic review to compile existing incidence data on toxins. The burden of disease associated with toxins will probably be reported only for the countries that have readily available estimates.

4.1.9 Hepatitis A

Tim Nguyen (WHO) and David Rein (University of Chicago) were consulted about GBD estimates related to hepatitis A. Concerns were raised about the transparency and repeatability of the GBD estimates. The WHO Hepatitis Group is currently generating estimates using alternative approaches. FERG will use the WHO results, which are expected to be available by early June. The final results should be published by September, which will mean that the estimates can be officially used by FERG, since they will have been peer-reviewed.

4.1.10 Norovirus

A systematic review of norovirus has been conducted by Hall et al. (unpublished work). During the EDTF meeting, it was decided that the norovirus estimates will not be corrected for isolation of norovirus from control samples. During FERG5, no key additional points or issues were identified.

The EDTF proposes to commission the Danish National Food Institute (DTU Food) to estimate the global incidence and mortality of diarrhoeal diseases caused by 11 foodborne hazards (eight enteric diseases and three parasitic diseases).

The project has the following overall objectives:

- to estimate the global and regional incidence and mortality of diarrhoeal disease caused by the agents *Shigella, Campylobacter, Salmonella, enterotoxigenic E. coli* (ETEC), *enteropathogenic E. coli* (EPEC), *Vibrio cholerae*, norovirus, "unknown diarrhoeal agents", *Cryptosporidium, Giardia lamblia* and amoebae in children under 5 years of age; and
- to estimate the global and regional incidence and mortality of diarrhoeal disease caused by the same agents in the population aged 5 years and over.

To accomplish these objectives, site visits will take place at the Nutritional Research Institute in Lima, Peru, and the Johns Hopkins University in Baltimore, Maryland, USA. The work will be performed between 15 April 2013 and 1 October 2013.

The deliverables of the commissioned work are:

1. a list of studies on the etiology of diarrhoea episodes and deaths in children under five years of age;
2. a list of studies on the etiology of diarrhoea episodes and deaths in older children, adolescents and adults;
3. country-level estimates of the proportion of diarrhoea episodes and deaths caused by the 11 named foodborne hazards in children under 5 years (to be delivered to the CTF);